

According to the present invention a functional equivalent of a CD163 variant or fragments thereof may be obtained by addition, substitution or deletion of at least one amino acid. When the amino acid sequence comprises a substitution of one amino acid for another, such a substitution may be a conservative amino acid substitution. Fragments of CD163 according 5 to the present invention may comprise more than one such substitution, such as e.g. two conservative amino acid substitutions, for example three or four conservative amino acid substitutions, such as five or six conservative amino acid substitutions, for example seven or eight conservative amino acid substitutions, such as from 10 to 15 conservative amino acid substitutions, for example from 15 to 25 conservative amino acid substitution. Substitutions 10 can be made within any one or more groups of predetermined amino acids.

Examples of fragments comprising one or more conservative amino acid substitutions including one or more conservative amino acid substitutions within the same group of predetermined amino acids, or a plurality of conservative amino acid substitutions, wherein each 15 conservative substitution is generated by substitution within a different group of predetermined amino acids.

One naturally occurring CD163 variant is the soluble CD163, that may be full length or truncated, such as shortened with the cytoplasmic tail and/or transmembrane segment 20

Accordingly, variant of CD163, or fragments thereof according to the invention may comprise, within the same variant of CD163, or fragments thereof, at least one substitution, such as a plurality of substitutions introduced independently of one another. Variants of CD163, or fragments thereof may thus comprise conservative substitutions independently of one another, wherein at least one glycine (Gly) of said variants of CD163, or fragments thereof of 25 CD163 is substituted with an amino acid selected from the group of amino acids consisting of Ala, Val, Leu, and Ile, and independently thereof, variant of CD163, or fragments thereof, wherein at least one of said alanines (Ala) of said variant of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Gly, Val, Leu, and Ile, and independently thereof, variant of CD163, or fragments thereof, wherein at least one valine (Val) of said variant of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Gly, Ala, Leu, and Ile, and independently thereof, variants of CD163, or fragments thereof, wherein at least one of said 30 leucines (Leu) of said variant of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Gly, Ala, Val, and Ile, and independently thereof, variants of CD163, or fragments thereof, wherein at least one isoleucine (Ile) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Gly, Ala, Val and Leu, and independently thereof, variants of CD163, or fragments thereof wherein at least one of said aspartic acids 35

(Asp) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Glu, Asn, and Gln, and independently thereof, variants of CD163, or fragments thereof, wherein at least one of said phenylalanines (Phe) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Tyr, Trp, His, Pro, and preferably selected from the group of amino acids consisting of Tyr and Trp, and independently thereof, variants of CD163, or fragments thereof, wherein at least one of said tyrosines (Tyr) of said variants of CD163, or fragments thereof of CD163 is substituted with an amino acid selected from the group of amino acids consisting of Phe, Trp, His, Pro, preferably an amino acid selected from the group of amino acids consisting of Phe and Trp, and independently thereof, variants of CD163, or fragments thereof, wherein at least one of said arginines (Arg) of said fragment of CD163 is substituted with an amino acid selected from the group of amino acids consisting of Lys and His, and independently thereof, variants of CD163, or fragments thereof, wherein at least one lysine (Lys) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Arg and His, and independently thereof, variants of CD163, or fragments thereof, wherein at least one of said asparagines (Asn) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Asp, Glu, and Gln, and independently thereof, variants of CD163, or fragments thereof, wherein at least one glutamine (Gln) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Asp, Glu, and Asn, and independently thereof, variants of CD163, or fragments thereof, wherein at least one proline (Pro) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Phe, Tyr, Trp, and His, and independently thereof, variants of CD163, or fragments thereof, wherein at least one of said cysteines (Cys) of said variants of CD163, or fragments thereof is substituted with an amino acid selected from the group of amino acids consisting of Asp, Glu, Lys, Arg, His, Asn, Gln, Ser, Thr, and Tyr.

It is clear from the above outline that the same variant or fragment thereof may comprise more than one conservative amino acid substitution from more than one group of conservative amino acids as defined herein above.

Conservative substitutions may be introduced in any position of a preferred predetermined CD163 variant or fragment thereof. It may however also be desirable to introduce non-conservative substitutions, particularly, but not limited to, a non-conservative substitution in any one or more positions.

A non-conservative substitution leading to the formation of a functionally equivalent fragment of CD163 would for example i) differ substantially in hydrophobicity, for example a hydro-

phobic residue (Val, Ile, Leu, Phe or Met) substituted for a hydrophilic residue such as Arg, Lys, Trp or Asn, or a hydrophilic residue such as Thr, Ser, His, Gln, Asn, Lys, Asp, Glu or Trp substituted for a hydrophobic residue; and/or ii) differ substantially in its effect on polypeptide backbone orientation such as substitution of or for Pro or Gly by another residue; and/or iii) differ substantially in electric charge, for example substitution of a negatively charged residue such as Glu or Asp for a positively charged residue such as Lys, His or Arg (and vice versa); and/or iv) differ substantially in steric bulk, for example substitution of a bulky residue such as His, Trp, Phe or Tyr for one having a minor side chain, e.g. Ala, Gly or Ser (and vice versa).

10 Substitution of amino acids may in one embodiment be made based upon their hydrophobicity and hydrophilicity values and the relative similarity of the amino acid side-chain substituents, including charge, size, and the like. Exemplary amino acid substitutions which take various of the foregoing characteristics into consideration are well known to those of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

15 The addition or deletion of an amino acid may be an addition or deletion of from 2 to preferably 10 amino acids, such as from 2 to 8 amino acids, for example from 2 to 6 amino acids, such as from 2 to 4 amino acids. However, additions of more than 10 amino acids, such as additions from 10 to 200 amino acids, are also comprised within the present invention.

20 It will thus be understood that the invention concerns CD163 variants comprising at least one fragment of CD163 capable of binding at least one Hp-Hb complex, including any variants and functional equivalents of such at least one fragment.

25 The CD163 variant according to the present invention, including any functional equivalents and fragments thereof, may in one embodiment comprise less than 1000 amino acid residues, such as less than 950 amino acid residues, for example less than 900 amino acid residues, such as less than 850 amino acid residues, for example less than 800 amino acid residues, such as less than 750 amino acid residues, for example less than 700 amino acid residues, such as less than 650 amino acid residues, for example less than 600 amino acid residues, such as less than 550 amino acid residues, for example less than 500 amino acid residues, such as less than 450 amino acid residues, for example less than 400 amino acid residues, such as less than 380 amino acid residues, for example less than 370 amino acid residues, such as less than 360 amino acid residues, for example less than 350 amino acid residues, such as less than 340 amino acid residues, for example less than 330 amino acid residues, such as less than 320 amino acid residues, for example less than 310 amino acid